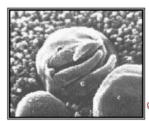
An Integrated Apicomplexan Parasite Database

Jessica Kissinger (Univ. Georgia) David Roos (Univ. Pennsylvania) Chris Stoeckert (Univ. Pennsylvania)





PlasmoDB is the official database of the malaria parasite genome project. This resource provides access to finished sequence for Pikamodium Naki/Namm/Istrain 3D7), generated by the Sanger Institute, TIGRINMRC, and Stanford, in addition to a wide range of related genomic-scale datasets from other sources. Publications exploiting PlasmoDB should provide appropriate acknowledgement to the database developers and those cientists who have made their data available on this site (see Acknowledgements and Publications). Development of PlasmoDB has been supported by the Burroughs Wellcome Fund



Release 2.2

Data Release: 2003/05/26

CryptoDB

The Cryptosporidium Genome Resources

Release 1.0 Data Release: 2003/01/14

CryptoDB provides access to the draft sequence for the genome of C. paysum (type land li). generated by VCU and MINESSOTA, as well as additional C. parsum data from various other sources (see Acknowledgements). Data are available for browsing, querying, and datamining subject to the Data Release Policy.

➤ Finished sequence and annotation released.

▶ PlasmoDB 4.0 released More News

Quick Links:

Browser Settings

- Tutorials
- ▶ Publications ▶ BLAST
- Sequence Retrieval Too
- ▶ Download Sequences

P. falciparum \$ 1.90!

Features:

Find an Annotated Gene by V

Welcome to Plasmo

PlasmoDB 4.0 provides a greatly enhanced a with publication of the complete parasite ge: PlasmoDB 4.0 incorporates DNA sequence sequencing centers (Nature 419:498-511); au algorithms; cDNA sequences (mapped to the motifs, T-cell epitopes, etc; cross-species co optical and genetic mapping data; population generated by a variety of complementary str information relevant to malaria research. A v manipulation, ePCR, BLAST searching, mot mass fingerprinting, etc. PlasmoDB is based a rich schema, enabling sophisticated queries

The blue navigation bar provided at the top (components of PlasmoDB. The forms provi access some of the most commonly used pag with questions, problems, and suggestions for Click here to see a list of features that we ex-

The Toxoplasma Genome Resource

ToxoDB provides access to the draft sequence for the genome of T. grandiii (ME49, atype II strain), generated by TIGR, as well as additional T. grand// data from various other sources (see Acknowledgements). Data are available for browsing. querying, and datamining subject to the Data Release Policy.

Welcome to ToxoDB 2.2

This database includes unfinished genome sequence data. Analysis of unfinished data poses many difficulties. In particular, some of the data has not been filtered to remove vector, bacterial, host or other contaminating sequences!

WARNING:

As of 05/26/03, 14:30 EST the new release of ToxoDB is up (after last-minute work done from Tarrytown, NY!). However, please note that this site is up without much testing. So, please be patient, send email to report bugs, and watch for corrections. Thanks!

Quick Links > Tools > Help ▶ Sequence Retrieval Tool BLAST · Tutorial on ToxoDB (SRT) · Find a Protein Motif Sequence Naming Convention Gene2EST **Download Bulk Sequence** GO! · Lutefisk · Frequently Asked Questions EMOWSE · What's New **Download Single Sequence:** Known Bugs Queries > sequence ID TGG_1095 Methods · Text Search End 200 · Acknowledgements Start 1 How to cite ToxoDB and Browse the Data > Organellar Data Sources Plastid \$ GO. Genome: · Data Sources ApiESTDB new NIAID Biomedical Resource Center Contract · Medline Toxo Updates

· Toxo Links

ome to CryptoDB 1.0

wse the Data >

ncludes unfinished genome sequence data. Analysis of poses many difficulties. In particular, some of the data has not remove vector, bacterial, host or other contaminating sequences!

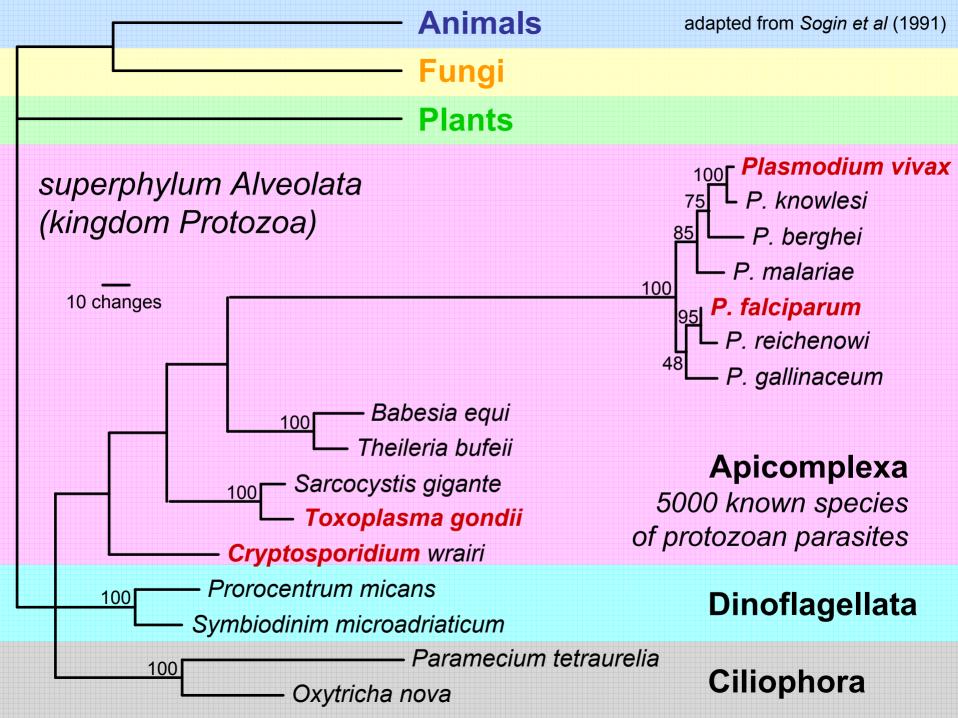
Help ▶ AST Tutorial on CryptoDB nd a Protein Motif Sequence Naming Convention ries > Frequently Asked Questions xt Search What's New new

Kick-off meeting, Rockville MD -- X/12-13, 2004

- Methods ta Sources Acknowledgements edline Cryptosporidium
- Data Sources yptosporidium Links

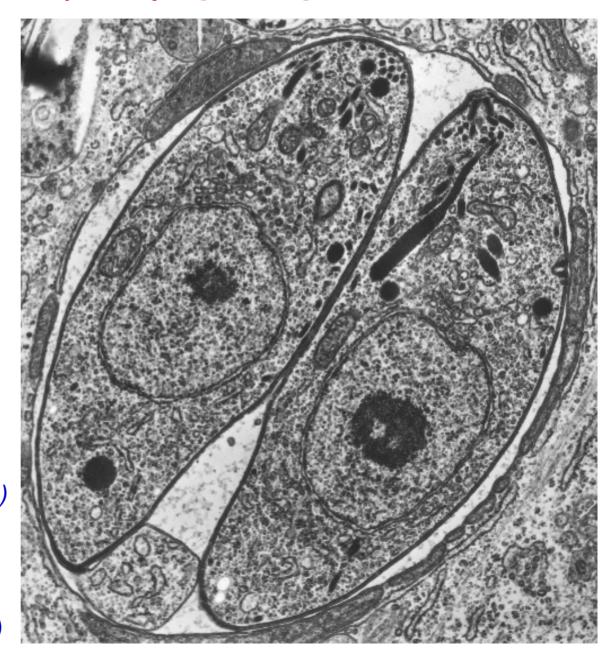
How to cite CryptoDB and

· Known Bugs



Distinctive Features of (most) Apicomplexan Parasites

- Complex developmental life cycle involving temporal differentiation, latent cysts
- Intracellular pathogen; parasitophorous vacuole mediates interaction with the host cell
- Replicates by assembling daughter parasites within the mother (schizogony)
- Standard eukaryotic machinery, plus unusual organelles:
- rhoptries & micronemes (for host cell attachment/invasion)
- conoid (apical cytoskeleton)
- inner membrane complex (assembly of daughter cells)
- apicoplast (2° endosymbiont)

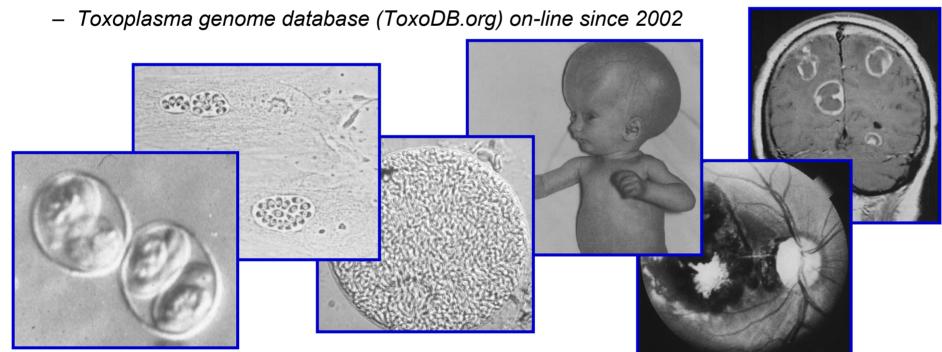


Cryptosporidium species – class B biodefense agent

- Biology: common intestinal pathogen
- Clinical: immunosuppressed individuals, no treatment
- Research: laboratory study extremely difficult
- Genomics (and beyond)
 - 9 Mb C. parvum sequence completed;
 C. hominis sequence effectively complete
 - <u>highly</u> reduced metabolic pathways; many horizontally-transferred genes including potential drug targets); multiple transporters
 - few ESTs (~1K); arrays in planning?; proteomics difficult
 - Cryptosporidium genome database (CryptoDB.org) on-line since 2004

Toxoplasma gondii – class B biodefense agent

- Biology: ubiquitous human pathogen
- Clinical: congenital infection, immunosuppressed individuals
- Research: accessible model organism
- Genomics (and beyond)
 - − ~65 Mb reference sequence effectively complete, seq. of two additional strains proposed
 - − ~100K ESTs, ~400K SAGE tags, representing all major strains, 3 life-cycle stages
 - cDNA-based glass slide arrays in use, photolithographic arrays under development
 - some proteomics data available, especially for apicomplexan-specific organelles



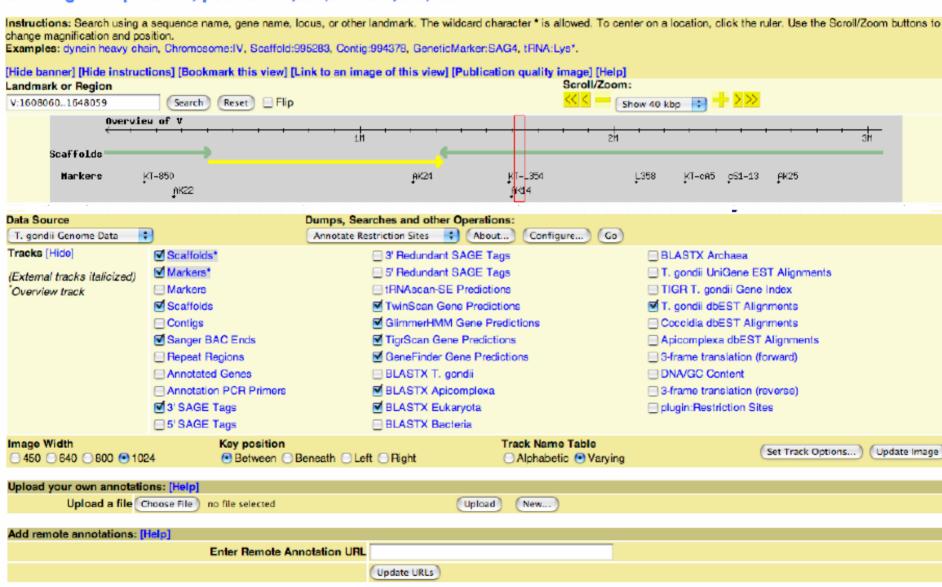


All data sources shown below are available for browsing, querying, and datamining, subject to the Data Release Policy.

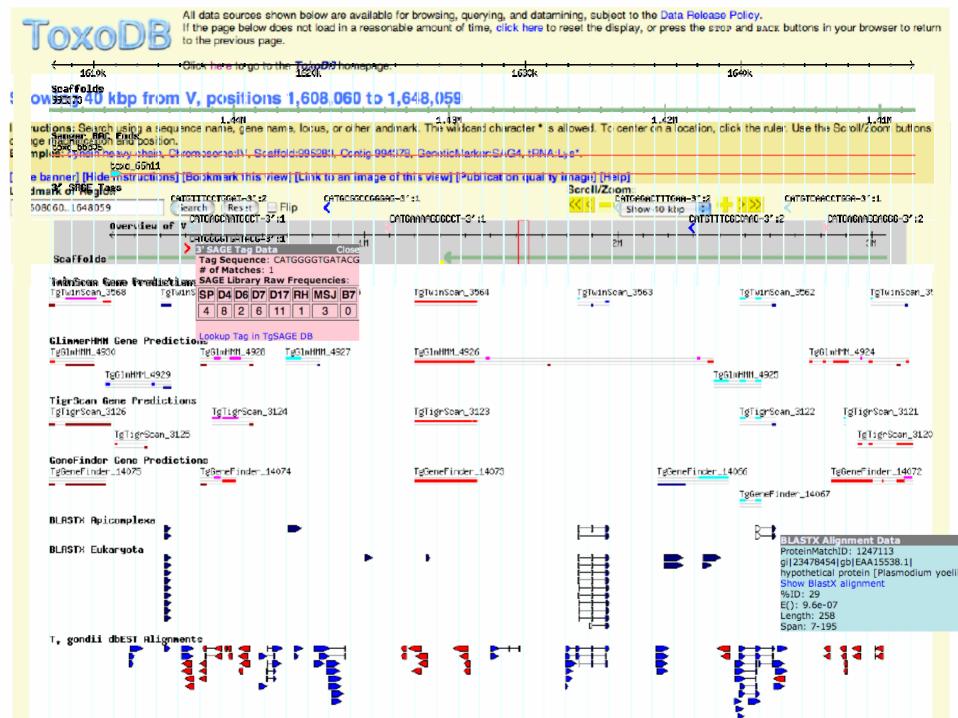
If the page below does not load in a reasonable amount of time, click here to reset the display, or press the stop and BACK buttons in your browser to return to the previous page.

Click here to go to the ToxoDB homepage.

Showing 40 kbp from V, positions 1,608,060 to 1,648,059

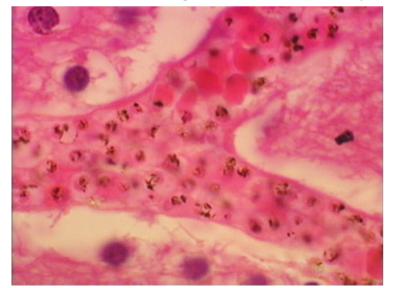


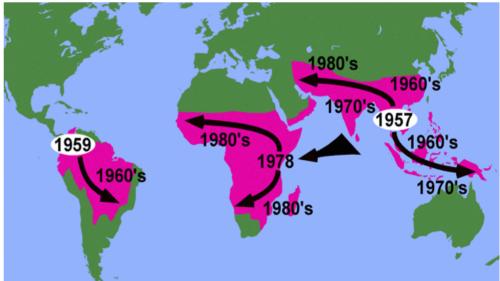
For the source code for this browser, see the Generic Model Organism Database Project. For other questions, send mail to help@toxodb.org



Plasmodium species – (re)emerging pathogens

- Biology: extreme specialist; important force in human evolution
- Clinical: problem acute & growing; drug-resistance, no vaccine
- Research: laboratory study now possible (but difficult)
- Genomics (and beyond)
 - 23 Mb genome P. falciparum sequence completed; complete sequencing of P. vivax in progress; 3-5X coverage available for several other species (P. berghei, P. chabaudi, P. gallinaceum, P. knowlesi, P. yoelii); sequencing of field isolate planned
 - 24K ESTs available for P.falciparum, 1K for P.vivax, 25K for rodent malaria species (P. berghei & P. yoelii); some SAGE tag data, high quality expression profiling data from both glass-slide and photolithographic oligonucleotide arrays
 - Plasmodium genome database (PlasmoDB.org) on-line since 2000







Release 4.1 Data Rolease: 01/23/2003

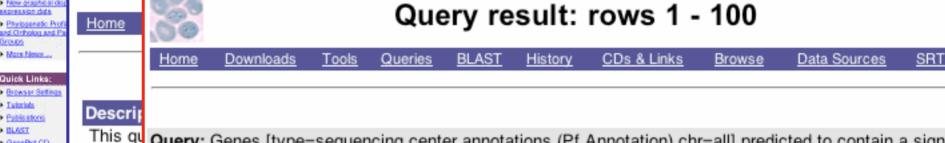
Candidate Vaccine Antigens query, part 1: secreted proteins

[1-100][10



Genes whose protein contains a predicted signal





Dountood Seque

Query

P. falciparum

 Querien: many different binds. combine results to be

· GenePiot CD

Vaccountilly in FACO Inc. first, and the methods we use to

[1-100][101-200]

Query

Run qu

Subm

Tools

Mitte

Query: Genes [type=sequencing center annotations (Pf Annotation) chr=all] predicted to contain a signal peptide.

Rows 1 - 100 of 651

location gene description PFA0025c pfal chr1: 53392-53503 VAR fragment, pseudogene

PFA0030c pfal chr1: 54001-55229 rifin

PFA0050c pfal chr1: 66050-67222 rifin PFA0060w pfal chr1: 71857-72659 hypothetical protein, conserved in P. falciparum

PFA0090c pfal chr1: 87436-88410 stevor PFA0095c 6 pfal chr1: 90475-91653 rifin

PFA0125c pfal chr1: 110984-116033 Ebl-1 like protein, putative PFA0135w pfal chr1: 124752-125719 hypothetical protein

PFA0180w pfal_chr1: 161365-166464 hypothetical protein

10 PFA0195w pfal chr1: 173099-174826 hypothetical protein PFA0210c pfal chr1: 183057-184457 hypothetical protein PFA0225w pfal chr1: 202774-204381 LytB protein



Release 4.1 Data Rolease:

Candidate Vaccine Antigens query, part 2: phylogenetic profile

Browse

hypothetical protein

hypothetical protein



Genes with a specified phylogenetic profile



SRT

Data Sources

Home

Query result: rows 1 - 20



the pro

ortholo

profil

BLAST Home Downloads Tools Queries History CDs & Links

Descri Quick Links: Putativ mosqu can be query

Query: All Pf genes with the following phylogenetic profile: A. thaliana=don't care C. elegans=don't care D. melanogaster=don't care E. coli=don't care H. sapiens=no S. cerevisiae=don't care A. gambiae=don't care musculus=don't care P. voelii=ves

Download Seque P. falciparum

Mors News...

Querien: Quer

ile.	[1	I-20][<u>21-40]</u>			Rows 1 - 20 of 2260	[1-20][<u>21</u>
ry		gene	ortholog group	group size	location	description
	1	PF11_0274	<u>755634</u>	2	chr11: 1027592-1028394	hypothetical protein
-1	2	PF10_0083	<u>755635</u>	2	chr10: 357345-358463	hypothetical protein
	3	PF11_0275	<u>755637</u>	2	chr11: 1029975-1034081	hypothetical protein
	4	PF10_0151	<u>755639</u>	2	chr10: 621303-623624	hypothetical protein
-1	5	MAL6P1.56	<u>755641</u>	2	chr6: 272734-274282	ST kinase, putative
-1	6	PF10_0154	<u>755642</u>	2	chr10: 633681-635285	ribonucleotide reductase small subunit, putative
	7	PFE0155w	<u>755644</u>	2	pfal_chr5: 130453-133392	hypothetical protein
	8	PF11_0204	<u>755645</u>	2	chr11: 742488-743546	hypothetical protein

chr6: 576383-577498

1293712-1295110

chr11:

Query

MAL6P1.298

10 PF11_0345

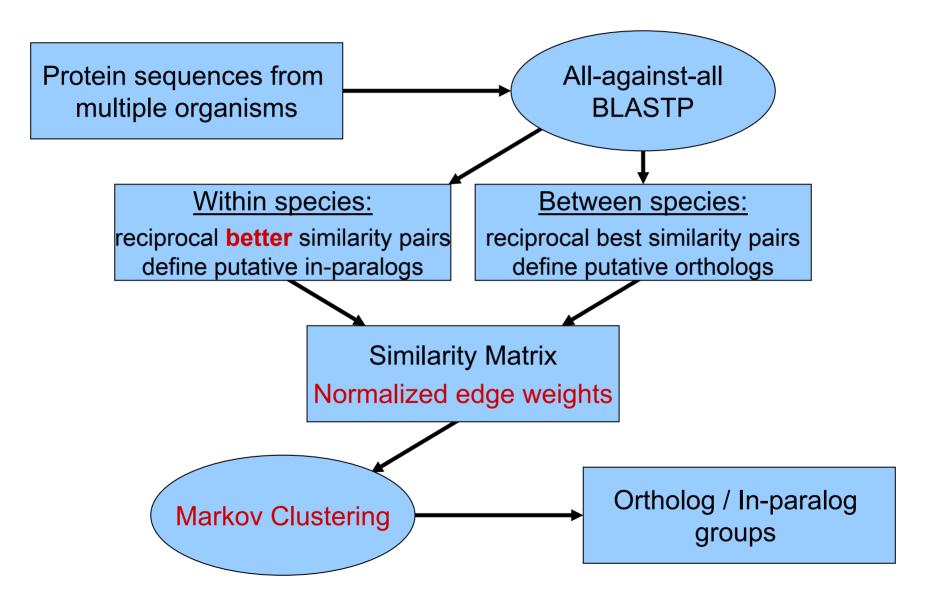
755647

755648

2

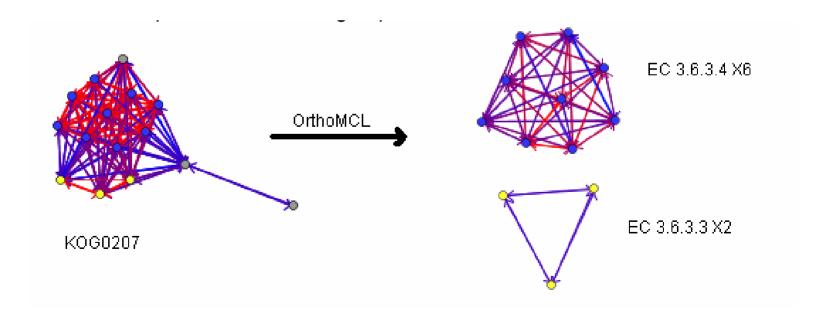
2

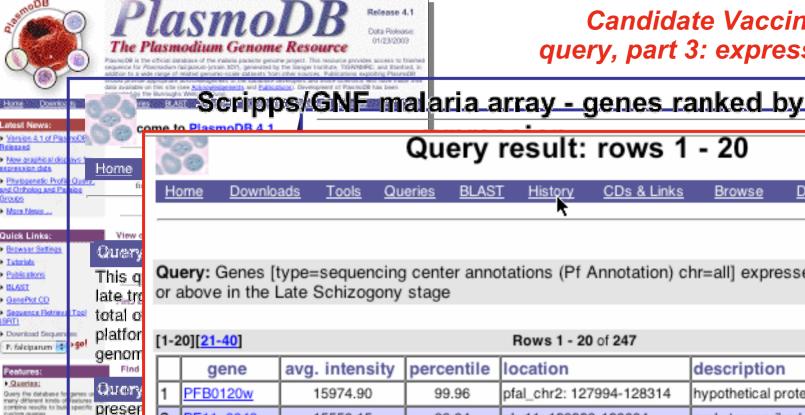
Identification of ortholog groups using OrthoMCL



EC-consistency of OrthoMCL and KOG groups

Methods	Total dataset		Groups with ≥2 proteins for which complete EC annotations are available			Consistent EC assignments		
meareac	groups	proteins (% of proteome)	groups	proteins	EC- annotated (% of total)	groups (% poss.)	proteins	EC-annotated (% possible)
OrthoMCL	13253	78998 (69)	998	10460	4122 (86)	886 (88)	8123	3495 (84)
KOG	10058	88645 (78)	926	14471	4393 (92)	772 (83)	9927	3359 (76)





13 PF11_0224

4332.25

99.73

Tools:

Download nucleotide and arrino acid sequences for P. Asicipanum and

This section contains bytorials on Practicable a FAQ list, news, a bug first, and the methods we use to percents the data.

POLY ! Ru

Candidate Vaccine Antigens query, part 3: expression profile

Browse

CDs & Links



Data Sources

circumsporozoite-related antigen

SRT

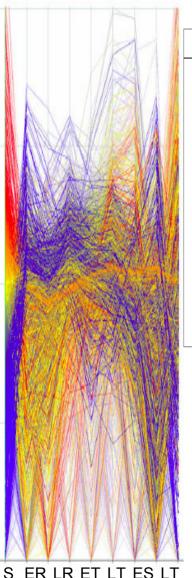
Query result: rows 1 - 20

History

		ype=sequencing _ate Schizogony		tations (Pf Annotation) c	hr=all] expressed in the 95th perce
0.	above in the E	ate cernzegeriy	otago		
[1	-20][<u>21-40]</u>			Rows 1 - 20 of 247	[1-20]
Г	gene	avg. intensity	percentile	location	description
1	PFB0120w	15974.90	99.96	pfal_chr2: 127994-128314	hypothetical protein
2	PF11_0040	15559.15	99.94	chr11: 129320-129604	early transcribed membrane protein 11.2
3	PFB0300c	8217.25	99.92	pfal_chr2: 273689-274507	merozoite surface protein 2 precursor
4	PF10_0372	6192.70	99.90	chr10: 1508412-1509473	hypothetical protein
5	PF13_0058	5204.35	99.88	chr13_1: 426154-426585	hypothetical protein
6	PF14_0598	5187.70	99.86	chr14: 2558046-2559295	glyceraldehyde-3-phosphate dehydrogen
7	PF10_0019	5053.90	99.84	chr10: 81417-81740	early transcribed membrane protein
8	PFC0120w	4901.05	99.82	pfal_chr3: 132097-137339	Cytoadherence linked asexual protein, Cl
9	PFA0420w	4622.80	99.80	pfal_chr1: 350323-350862	hypothetical protein
1	0 <u>PFE0165w</u>	4435.15	99.79	pfal_chr5: 140710-141471	actin depolymerizing factor, putative
1	1 MAL13P1.308	4349.45	99.77	chr13_1: 2369502-2377598	hypothetical protein
1:	2 PF11 0039	4346.10	99.75	chr11: 126406-126681	early transcribed membrane protein 11.1

chr11: 813000-813936

Available microarray datasets spanning the P. falciparum intraerythrocytic life cycle



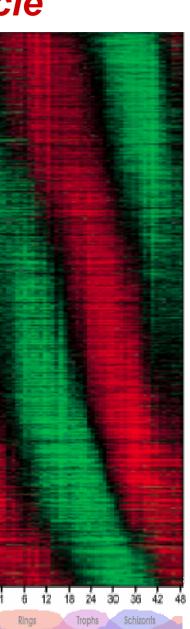
M G

	Le Roch et al	Bozdech et al
Array Platform	Custom Affy	Glass Slide
Oligos Mapped to Pred Coding Seq	260,596	7462
Oligos Mapped to Pred Non-coding Seq	106,630	None
Average # of Oligos Used per Gene	17.4	1.3
Genes for which Data is Available	5104	4372
Erythrocytic Time Points	6 + 6	48 + 50 + 53
P. falciparum Strain	3D7	HB3/DD2/3D7
Synchronization Method	Sorb/Temp	Sorbitol
Erythrocytic Oligo-level Data Points	4,406,712	1,126,762
Erythrocytic Gene-level Data Points	61,248	660,172

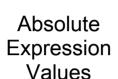
How to compare?

Le Roch, KG, Y Zhou, PL Blari, M Grainger, JK Moch, JD Haynes, P De La Vega, AA Holder, S Batalov, DJ Carucci & EA Winzeler (2003) Discovery of gene function by expression profiling of the malaria parasite life cycle. Science **301**:1503-8

Bozdech, Z, M Llinas, BL Pulliam, ED Wong, J Zhu & JL DeRisi (2003) The transcriptome of the intraerythrocytic developmental cycle of Plasmodium falciparum. PLoS Biol. **Epub:** Aug 18.

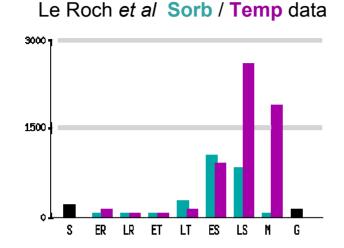


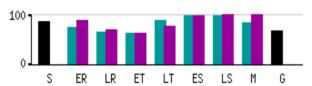
Comparing expression profiles across platforms

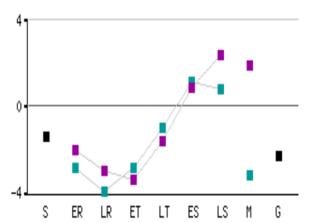


Percentiled Expression Values

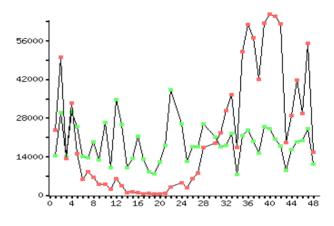
Fold Induction/Repression (log ratio expression)
GS: log₂(red / green)
Affy: log₂(x_i / ave[x])



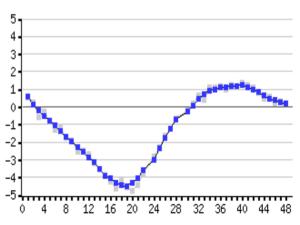




Bozdech et al strain HB3 data



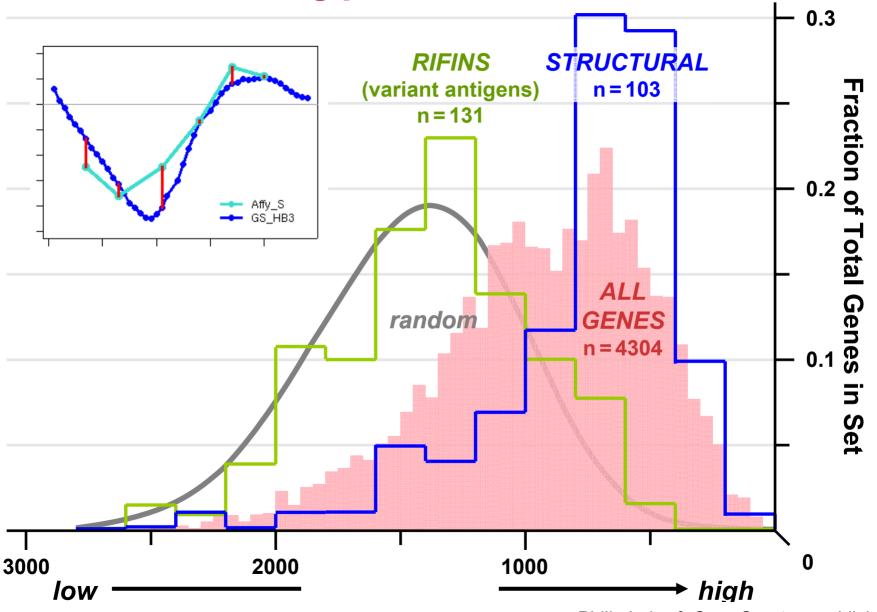




Philip Labo & Greg Grant, unpublished

Example: MSP1

Assessing profile concordance





Candidate Vaccine Antigens

Browse

Downloads

Tools



Query History



SRT

Data Sources

Home

Query result: rows 1 - 20

BLAST

Release 4.1

Data Rolease: 01/23/2003

Queries



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This page below you intersect.

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Download Seque P. falciparum

Querien:

Mors News ...

Quick Links:

Browser Setting Interiors

first, and the methods Follow on

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Gen chr= Sch

10

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buttons to create a r appearing UN

[1-20][21-26] Rows 1 - 20 of 26 [1-20][2 Query: ((All Pf genes with the following phylogenetic profile: A. thallana=don't care C. elegans=don't care in general care don't care in general care don't care in general care don't care don't care in general care don't care don' pypothetical people encing center annotations (Pf Annotation) ptal-shubalita957s184457sect (Ge ofal chr2: 522931-523999 hypothetical protein PFB0570w imatisp) 255=all:1685588866575359 95th percer||Pesakabayainsthan-atanSchizocanyaf2866cursor PFE0370c pfal_chr5: 307490-309556 subtilisin-like protease precursor, putative 5-2(PPE8095c R Woothetical protein [1-20][2 ofal_chr5: 328666-329715 pfal_chr5: 1301219-1301764 early transcribed membrane protein PFE1590w RE8828857 2648C52765836579594457 hveethetical eretein PF07 0128 chr7: 1265975-1270488 erythrocyte binding antigen

hypothetical protein

hypethetical pretein

merozoite surface protein 1, precursor

History

CDs & Links

PF10_0119 chr10: 470978-471932 887719929876747292635

MALSPIRA

PFI1270w

PETANO

PF11475w

IRE0026957

PF10_0372 chr10: 1508412-1509473

caro: 544240-545252

pfal chr9: 1040703-1041506

sfal_ent5; 14959994986497

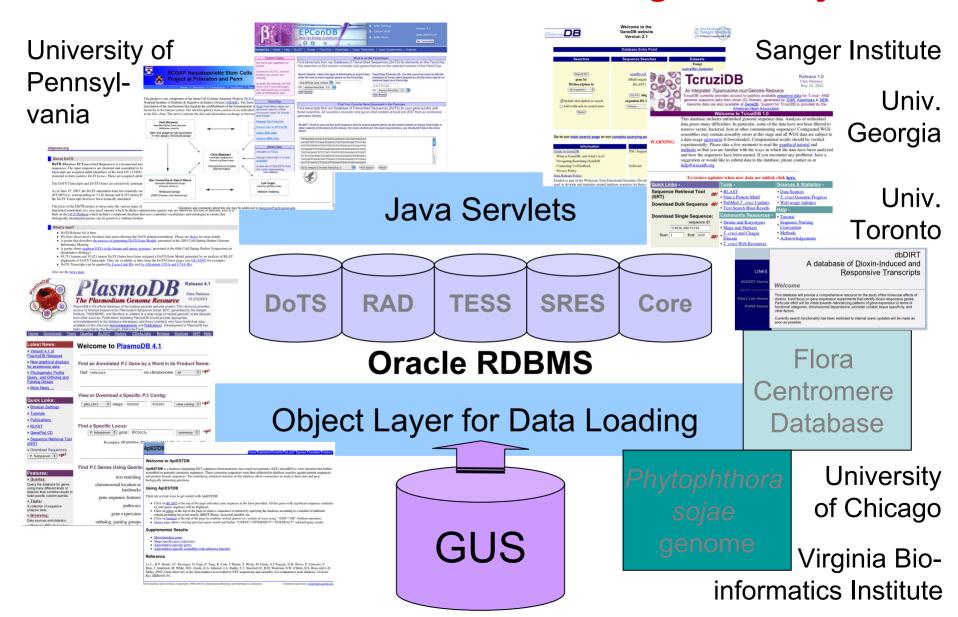
ofal chr9: 1201802-1206964

6taP ch73527073872747.87

rkastretratene tutativa hypothetical protein axical membrane antigen 1 precursor hypothetical protein

Rissandiga falsigarum membrane protein pf12 precursor

The Genomics Unified Schema (GUS): A Functional Genomics Data Management System



GUS: Genomics Unified Schema http://www.gusdb.org

Namespace	Domain	Features	
DoTS	Sequence and annotation	EST clusters Gene models	
RAD	Gene Expression	MIAME/MAGE-OM	
TESS	Gene Regulation	TFBS organization	
Sres	Shared Resources	Ontologies	
Core	Data Provenance	Documentation	

GUS Components

your data GenBank **NRDB** dbEST **SNPs** gene traps microarrays phenotypes pathways orthologs taxonomy GO SO EC and more ...

Pipeline API

Plugins (data loaders)

Data Load API

Perl Object Layer



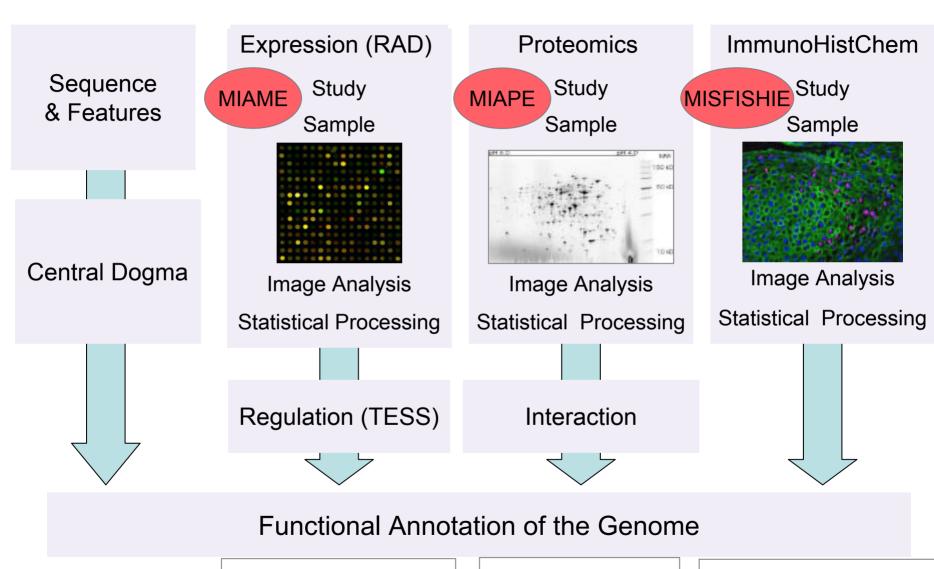


Web Development Kit

Queries & Analysis

Warehouse (Oracle or PostgreSQL)

Functional Genomics with GUS

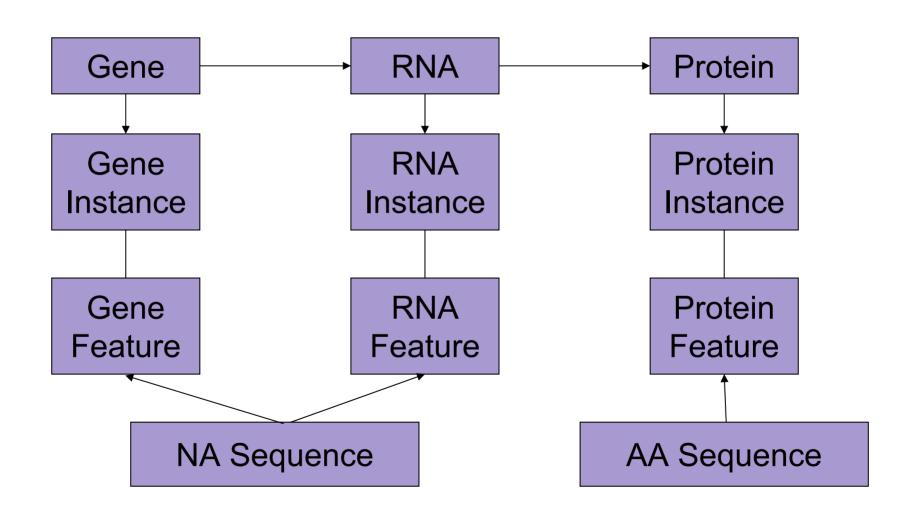


www.mged.org

psidev.sf.net

www.scgap.org

Central Dogma and Sequences



Finding all "kinases" in P. falciparum



Rows per

Run auerv

Submit --

page: 20

Reset

Genes with a GO function assignment



Tools Queries BLAST History CDs & Links Browse Data Sources Description This query allows one to retrieve all the genes that share the same predicted GO gene function Query parameters Chromosome: all -Query result: r mon-summ electron transfer carrier too. isocitrate dehydrogenase (GO:0004448) isocitrate dehydrogenase (NADP+) (GO:0 Home Downloads isoleucine-tRNA ligase (GO:0004822) isomerase (GO:0016853) GO Function: kinase (GO:0016301) Query: Genes [type=Pf sequencing center annotal kinase inhibitor (GO:0019210) function 'kinase (GO:0016301)' combine the selected queries as follows: kinase regulator (GO:0019207) kinesin motor (GO:0016326) [1-20][21-40] Rows 1 - 20 of 1 lactate dehydrogenase (GO:0004457) UNION INTERSECT lactovialutathione lyace (CO:0004462) Pf sequencing center annotations Results will appear as a new query. Query options

	[1-2	0][21-40]		KOWS 1 - 20 01 1
		gene	location	descripti
	1	PFA0130c	pfal_chr1: 119275-121648	Serine/Three
	2	PFA0380w	pfal_chr1: 315774-320559	serine/threo
	3	PFA0515w	pfal_chr1: 406893-413323	phosphatidy
	4	PFA0555c	pfal_chr1: 440804-442570	UMP-CMP1
	5	PFB0150c	pfal_chr2: 149524-159660	protein kina
	6	PFB0520w	pfal_chr2: 469790-473491	protein kina
	7	PFB0605w	pfal_chr2: 541811-543807	Ser/Thr prot
	8	PFB0665w	pfal_chr2: 594196-599340	Ser/Thr prot
	9	PFB0815w	pfal_chr2: 720436-722660	protein kina
	10	PFC0060c	pfal_chr3: 74873-77071	Serine/threo
ı	11	PFC0105w	pfal_chr3: 110750-114766	serine/threo
	12	PFC0385c	pfal_chr3: 385812-391279	serine/threo
	13	PFC0420w	pfal_chr3: 419053-421354	calcium-dep
	14	PFC0485w	pfal_chr3: 485480-493186	protein kinase

Query History



This page displays queries you have run in the current session. Use it to link back to the result sets of those queries, or to combine them into new result sets. Jump to the most recent query.

Click to Select	Query			Download	Size
	Genes [type=Pf sequencing center annotations chr=all] predicted to have GO function 'kinase (GO:0016301)'	11:16:23 AM	view	Data Download	104

To view results, click on "view" to the right of the desired query.

To download data, click on "data download", which will allow you to retrieve sequence data in FASTA format, or to select types of data to retrieve in a custom report

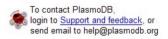
To combine data, first choose the queries of interest by clicking the check boxes at left, then

TOP MINUS BOTTOM BOTTOM MINUS TOP

Or DELETE the selected query results from your query history.

Union includes any genes identified by any selected query. Intersect includes only those genes identified by every selected query. Top Minus Bottom identifies genes in the first set that are not in any subsquent set checked. Bottom Minus Top includes genes in the last query checked that are not in previous queries selected.

Plasmodium Sequence Release Date: 2003/11/04



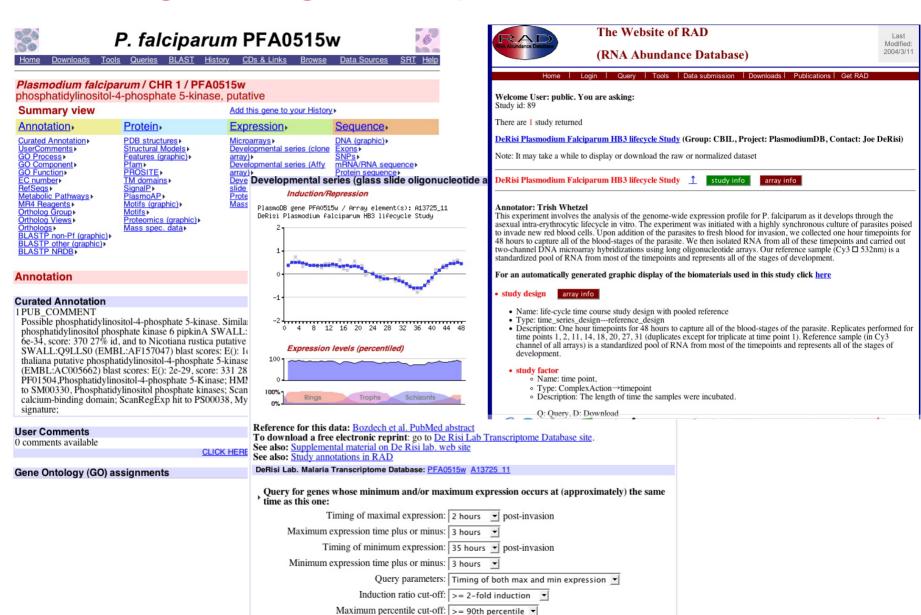
Plasmodium Sequence Release Date: 2003/11 Place a DB Date: 2004/07/15 e, putative 15 PFC0525c pfal chr3: 520829-523002 glycogen synthase kinase, putative 16 PFC0755c pfal chr3: 686827-691488 protein kinase, putative 17 PFC0945w pfal chr3: 891430-892781 protein kinase, putative 18 PFD0740w pfal chr4: 688793-692951 Plasmodium falciparum protein kinase, putative 19 PFD0755c pfal chr4: 696623-697312 adenylate kinase l

pfal chr4: 794224-796323

20 PFD0865c

cdc2-related protein kinase 1

Gene Pages Integrate Sequence with Functional Gx



Run query: Run query

The RAD Study Annotator



From Assay to Quantification

- Assay

-- Hybridization Parameters

Annotation by

user: stoeckrt

project: Testing

group: Testing

study: Sample Study (private)

- Image Acquisition
- -- Image Files
- -- Acquisition Parameters
- Image Quantification
- -- Raw Data Files
- -- Quantification Parameters
- Summary

Study/Experiment*

(* MGED Core Ontology)

- Study Design
- -- Study Design Assay
- Study Factor
- -- Study Factor Value

- Summary BioMaterial

- Existing BioMaterials
- BioSource
- BioMaterial Characteristics
- Treatments
 - -- Sample pooling
 - -- Sample splitting
 - -- Labeling
 - -- Other treatments
 - -- Treatment parameters
- AssayLabeledExtract

Summary

Miscellaneous

- Contact
- Protocol

RAD Study-Annotator

To access the tutorials click here

Satisfies the MIAME checklist, using the MGED Ontology

Allows entering very specific experimental details

Web-based forms:

Modular structure

Written in PHP

Front-end data integrity checks using JavaScript

Manages data privacy, based on project & group selections in GUS schema

Obtaining and Using GUS; Visions for the Future

- see <u>www.gusdb.org</u>; more info at <u>www.gusdb.org/documentation</u>
- active gusdev mailing list
- relatively straightforward to install, but loading data can be a struggle
 - growing number of tools available
 - addressing how to use and write tools with visits
 - improve 'install' scripts, documentation
 - postgres version
- Web Development Kit (WDK) to generate web sites on GUS
- extendable to all areas of functional genomics
 - sequence & array-based expression experiments
 - array CGH, 2D gel electrophoresis, MS, yeast-2-hybrid data, etc
 - *in situ* hybridizations, metabolites
- Interoperability with other GUS installations and common tools
 - exchange files and scripts, MAGE-ML (use community standards
 - web services (exchange objects)
 - interface with open source tools (Gbrowse, Artemis, Apollo, etc)

Plans for ApiDB

- Separate GUS installations for PlasmoDB, ToxoDB, CryptoDB, and ApiDoTS (to become ApiDB)
 - each project on its own release schedule
 - common download repository for synchronizing third-party data
- Web portal providing queries across resources
 - web services to federation of GUS installations
 - queries based on common relationships
 - GO assignments
 - Ortholog and paralog groups
 - E.C. assignments and pathways
 - etc